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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,113	SACHS ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *21 February 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) *1,3,15,25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence letter.*

DETAILED ACTION

Claims 1-27 are pending.

Priority

1. No priority claim has been made.

Information Disclosure Statement

2. The information disclosure statements (IDS) submitted on June 17, 2002 and August 4, 2003 have been considered by the examiner.

Sequence Letter

3. Applicant is given the time period set forth for this letter to comply with the sequence rules. Please see Notice to Comply attached hereto.

4. Claim 2 and 27 set forth amino acid sequences, which have not been identified with a sequence identifier. The sequences set forth in these claims do not comply with the Sequence Rules which require any amino acid sequence of 4 amino acids or more to be identified with a SEQ ID NO identifier.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. What is now claimed is a composition that reads on a bacteria in nature that comprises the recited proteins. The proteins of claims 1-2, 4, 6 have not been isolated and purified, especially in light of claim 3 which states that the claimed proteins are purified; therefore the claims that come before claim 3, assuming claim 3 is further limiting of claims 1-2, read on a product of nature. The claimed invention is directed to non-statutory subject matter, in light of the fact that bacterial cells are compositions that comprise a plurality of proteins, especially

Helicobacter pylori strains from which a purified protein can be obtained. This rejection could be obviated by amending claims 1-2 to recite the phrase ---isolated and purified--.

Claim Objections

7. Claim 1 is objected to because of the following informalities: Claim 1 requires "at least three proteins", and also defines the composition to be a single protein "is selected from the group consisting of"; the claim recites both the singular and plural tenses for the claimed invention setting forth a claim that is not internally consistent.

8. Claim 3 recites the phrase "are in purified state"; a transitional article –a—appears to be missing between "in" –a—"purified state".

9. Claim 15 recites the phrase "sample which specific"; a transitional article –is—appears to be missing between "which" –is--"specific".

10. Claim 25 sets forth a combination of claim limitations that lack transitional articles: "In a method for determination ?? (---determining eradication--- or ---of eradication---) the eradication of Helicobacter pylori the improvement consisting in???? (---consisting of detecting--) the detection of the presence or absence of antibodies resulting from Helicobacter pylori infection by a method according to claim 15, before, during and after eradication treatment."

Appropriate correction is required.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are is directed to compositions that comprises at least three proteins, the proteins comprising regions selected from another protein designated HP1, HP2, HP3 and HP4, HP1, HP2, HP3 and HP4 and defined to evidence a relative molecular weight of 32 kd, 30 kd, 23 kd and 15 kd respectively (independent claim 1), but what region or regions of HP1, HP2, HP3 and HP4 have been chosen to be a part of the claimed proteins has not been described. While specific species defined by complete amino acid sequences shown in claim 2 have been disclosed, what the claimed proteins are, that only comprise any region, a small portion of the sequences recited in claim 2, and additionally comprise unspecified amino acids to result in a protein of the required relative molecular weight antigen set forth in claim 1, the additional portions of the proteins having not been described.

The claimed proteins are required to have an antigenic functional characteristic to Helicobacter pylori, but the antigenic region of Helicobacter pylori has not been described by any specific monoclonal antibody, or to have any specific chemical structure, but only to comprise any region of the sequence that can be incorporated into a protein of the recited relative molecular weights and to be reactive with any antibody reactive with Helicobacter pylori. What has been claimed is a composition that contains within its scope a plurality of proteins that are homologs or analogs to Helicobacter pylori antigens that have a single common structural region, but no specific biological function other than a single antigenically cross reactive region.

Applicant also broadly describes the invention as embracing any substitution, insertion or deletion of amino acids throughout the entire stretch of amino acids found in the reference sequence by use of language in which only a region of HP1, HP2, HP3 and/HP4 is required, but the final relative molecular weight of the resultant protein is far larger than the region that can be selected from the reference proteins. Chen et al (1994) teaches that H.pylori urease (a protein that comprises an about 30 kd protein subunit) shares an antigenic region with Jack Bean Urease (see Chen et al, cites Clayton et al (reference 7 of bibliography) page 249, col. 1, "immunological cross-reactivity to exist between antibodies to jack bean urease and H.pylori and H.felis antigen", but the protein that shared an antigenic region did not serve to treat infection and would not serve to diagnose Helicobacter pylori infection because the immunoreactivity induced to H.pylori 30 kd protein inconsistently immunoreacts with the antigen of Chen et al which shares an antigenic region of the H.pylori 30 kd protein, a protein

now claimed. None of the proteins that comprise any antigenic region of the recited sequence and reacts with an anti-Helicobacter pylori antibody, but differs by any number of amino acids, and has a sequence not represented by the sequences of claim 2, comprise amino acid sequences that do not meet the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The claimed proteins that comprise sequences other than those set forth in claim 2, and only comprise an antigenic epitope of 3-10 amino acids out of a possible 266 amino acids (about 32 kd), fail to have an adequate written description in the instant specification. The specification does not provide original descriptive support for what the additional amino acid sequences are , that are in association with any number of regions selected from each of the recited HP proteins.

The skilled artisan cannot envision all the contemplated proteins that comprise any amino acid antigenic sequence region of HP1, HP2, HP3, or HP4. The detailed chemical structure of the claimed genus of proteins has not been described and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. A method of screening for antigenic immunoreactivity is not a method of making a protein, the product itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. . Thus, the written description of the instant specification does not provide for "comprising" language. In the instant case the specification provides only written description for a proteins comprising any region of the protein sequences set forth in claim 2, other than the proteins defined by the amino acids sequence of claim 2. Therefore, only isolated proteins of SEQ ID Nos for the sequences of claim 2 have been described but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that

the written description provision of 35 USC 112 is serviceable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

13. Claims 1-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, and claims 2-27 which depend therefore, recite the phrase "comprising regions which act as antigens specific to Helicobacter pylori". As a genus of embodiments that define a plurality of regions that act as antigens representative of the pathogen Helicobacter pylori but are not Helicobacter antigens have not been defined or disclosed, what the "regions" are that "act as antigens specific to Helicobacter pylori" are not distinctly claimed. The term "specific" is a relative term that can imply low specificity, high specificity , or cross-reactivity, but is also specific for Helicobacter pylori. The relative functional limitation "specific" used to define any structural region, does not distinctly claim Applicant's invention.

Claim 5 recites the phrase "which is a combination and not a mixture of said proteins." How can a combination of proteins not be a mixture? When proteins are combined to form a single composition, the proteins are mixed together. What is claimed appears not to be a composition, as a composition is a combination of components that are in association with each other, and need not be uniformly mixed together, but forms a mixture of components, through the presence of more than one component in the composition, thus defining a composition that comprises a mixture. Claim 5 is unclear. Clarification is requested.

Claim 7 should recite—further comprises a suitable solid phase to which said proteins are attached--.

Claim 8 should recite ---further comprises membranes in said microtiter plate to which the proteins are attached---. Claim 8 depends from claim 7 which defines the solid phase to be a plate, and claim 8 seeks to define the solid phase to be something other than a plate, specifically a membrane. The combination of claim limitations is not internally consistent. Clarification of the invention is requested.

Claim 11 defines the proteins to be "on a test strip" and depends from claim 7 which defines the proteins to be "attached to a suitable solid phase". The proteins "on a test strip" does not require the proteins to be attached to the test strip, which is a requirement of claim 7. The combination of claim limitations set forth in claim 7 and claim 11 are confusing because where or how the proteins interact (on or attached) with a solid phase or test strip are differently expressed. Clarification of the invention is requested.

Claim 12 is directed to a method of preparing the composition of claim 10, but does not result in a composition that comprises proteins attaches to the membranes (claim 9 claim limitations, from which claim 10 depends). Claim 12 does not recite an attaching step are required for the composition of claim 10. Claim 12 is directed to an incomplete method for preparing the composition of claim 10.

Claims 15-19 are directed to a method of detecting active infection caused by Helicobacter pylori. Any level of antigen-antibody complex formation is claimed as being indicative of current Helicobacter pylori infection. Karnes et al (1991) teaches that antibodies present in serum samples reacted with Helicobacter pylori antigens in vitro, but no in vivo,

current active infection was found to be present based upon tissue staining samples from patients with atrophic body gastritis. The invention of claims 15-19 is not distinctly claimed in light of the fact that any level of antigen-antibody complex formation, with an antibody in a human serum sample, would not "denote the presence of Helicobacter infection" as the prior art (Karnes et al , 1991) shows that serum antibody reactivity does not denote "the presence of Helicobacter pylori infection".

Claim 24 should recite the phrase –further comprises a test strip—and –wherein the proteins are attached thereto—or phases that clearly set forth Applicant's invention. Is the test strip of line 1, the nitrocellulose membrane recited on line 2? The test strip and the composition and the nitrocellulose membrane are not so claimed as to be interconnected. Clarification of the inter-relationship of the recited components of the claimed composition is requested.

Claim 24 also recites the phrase "antibody is used for detection". This phrase does not positively set forth the presence of the antibody in the claimed kit through the recitation of future tense "use" process language. The process language "is used" does not require the presence of the gold labeled antibody to be in the kit. What components are intended to be in the claimed kits? The invention is not distinctly claimed.

Claim 25 seeks to set forth a Jepsen claim, that defines the "improvement " to be "the detection of the absence of antibody resulting from Helicobacter pylori infection by a method according to claim 15, before, during and after eradication treatment. It appears that the claim defines the improvement to be measurement of the **absence** of anti-Helicobacter pylori antibodies at all three points in the treatment of Helicobacter pylori infection. How would the absence of Helicobacter pylori antibodies before, during and after eradication treatment be an

improvement ? The word "absence" lacks antecedent basis in claim 15, which recites the term "presence". The invention is not distinctly claimed.

14. Claims 26 and 27 are directed to a method of **using** a combination of at least three proteins, but no active voice methods steps are set forth in the claim. The phrase "for detecting" defines a recited intended use of the at least three proteins, but is not a methods step. Claims 26-27 provide for the use of at least 3 proteins, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 26-27 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002

do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

16. Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Antoljak et al (1998).

Antoljak et al disclose "In a method for determination the eradication of Helicobacter pylori the improvement consisting in the detection of the presence or absence of antibodies resulting from Helicobacter pylori infection by a method according to claim 15, before, during and after eradication treatment", wherein the reference measured anti-HP IgG during Helicobacter pylori eradication (see title), through monitoring antibody levels utilizing an ELISA before (see abstract, line 7), during (see abstract, line 6) and after (see abstract line 10) triple eradication therapy (see narrative bridging lines 7-8, abstract).

The methods steps of claim 15 to which claim 25 refers, recite a combination of steps which were carried out before, during and after eradication treatment, the steps comprising:

contacting the sample with a composition,

permitting the sample and the composition to form an antigen/antibody complex; and

detecting the presence of the complex.

These three methods steps are disclosed and described in the method of Antoljak et al, wherein the sample was plasma, the composition comprised Helicobacter pylori antigens of which there were at least three, and the complexes formed were detected based upon titer determinations (concentration of antibodies in a sample). The asserted improvement is anticipated by Antoljak et al.

17. Claims 15 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Bazillou et al (1994).

Bazillou et al disclose the instantly claimed invention directed to a method that comprises the steps of :

contacting a serum sample (rabbit serum sample, see page 311, col. 2, last paragraph) with a composition that comprises at least three Helicobacter pylori proteins (see Figure 1, extracted H.pylori antigen containing material);

permitting the sample and the composition to form a complex (see page 312, Figure 1, labeled complexes shown); and

detecting the complex with a gold labeled antibody to detect the antigen/antibody complex (see page 312, col. 1, paragraph 1, and figure 1 at top of page 312). The reference anticipates the instantly claimed invention.

18. Claims 1-2, 20 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Chandler (US Pat. 6,128,956).

Chandler discloses the instantly claimed composition and kit that comprises a device that is utilized as an analytic tool in the physician's office (see col. 2, lines 27-33), the device being a type of kit for sample analysis, wherein Helicobacter pylori specific antigens (see Example 4, line 41; Example 2, col. 5, lines 15-16, 23-24) are attached to a nitrocellulose solid phase (see col. 5, line 14) and a gold labeled antibody (see col. 5, lines 25-26) is used for detection. The reference inherently anticipates the instantly claimed invention.

19. Claims 1-13, 15, 19, 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Voland et al (April 1999).

Voland et al disclose a composition of Helicobacter pylori proteins designated HP1, HP2, HP3 and HP4 (second half of paragraph).

A first composition comprised at least three Helicobacter pylori proteins, and were present in a whole cell lysate from strains designated ATCC 43504, and isolated strains HP08 and Hp02. The proteins were used in an ELISA (microtiter plate) and in a Western blot (membrane based) solid phase based assays to which the proteins were attached through adherence.

A second composition comprised at least three H.pylori proteins, wherein the proteins were in combination together but not in a mixture through electrophesis and transfer of the proteins to a solid surface used for Western blotting (Methods section, first line) of the H.pylori proteins with patient sera (see method section line 3). The proteins were purified through separation from the native cell structure through generation of a whole cell lysate and Western blotting (see Methods section) on to a test strip (see Methods section). Inherently the reference anticipates the instantly claimed invention.

20. Claims 1-9, 11-12, 15-17, 19, 20-23, 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Pronovost et al (US Pat. Dec. 8, 1998).

Pronovost et al disclose the instantly claimed invention directed to a composition of at least three H.pylori proteins of a relative molecular weight of about 15, 23, 30 and 32 kd, wherein the proteins of Pronovost et al were 16, 21, 29 and 31 kd (see col. 13-14, claims 5-6), all relative molecular weights within the acceptable range of variability, and therefore anticipate claimed invention. The proteins were fractioned based upon SDS-PAGE gel electrophoresis, defining a composition of purified proteins that were in a single composition, but not in close association such as a mixture.

The composition of Pronovost et al also includes H.pylori proteins and reagents for carrying out the disclosed assays (see Pronovost et al, col. 5, lines 25-30) in kit form (see Pronovost et al, col. 6, lines 5-14). The kits comprise H.pylori derived proteins, attached (immobilized) on a suitable solid phase (solid support, see Pronovost et al, col. 14, claim 6). Among the solid phases disclosed for attachment of the H.pylori proteins include "an absorbent

pad placed in a molded bottom casing", a type of membrane (see Pronovost et al, col. 8, lines 29-31), ELISA testing in a microtiter plate (see Pronovost et al, col. 9, lines 42-43), red blood cells (see col. 12, claim 2, lines 42-47), lateral flow supports, and immunoblotting surfaces (see col. 5, lines 28), as well as latex , for latex agglutination (see abstract, middle of paragraph; and col. 5, lines 25-67).

Among the kit reagents that can be used to perform the methods of the invention (see col. 6, lines 6-9) are antihuman IgG antibodies (see col. 5, line 49), an enzyme substrate(see col. 5, line 51) and buffer solution (see PBS-Tween 20 (wash, col. 5, line 45), positive and negative control samples (see col. 8, lines 22-27; and col. 8, lines 43-62).

Additionally, Pronovost et al disclose a method of preparation of antigen and a method of detecting the presence of antibodies to Helicobacter . The method of preparation of antigen comprises the steps of:

preparing a lysate of a whole bacterial cell (see Example 1, sonicate) of Helicobacter pylori;
subjecting the lysate to gel separation (see Example 2, col. 7, lines 5-45)
transferring the proteins to membranes (see Example 3, especially col. 8, line 31).

The method of detecting the presence of antibodies comprises the steps of:

contacting the human serum sample (see col. 4, line 15) with a composition that comprises at least three Helicobacter pylori proteins (see claims 5-6);
permitting the sample and the composition to form a complex (bind, see col 5, line 50); and
detecting the complex with an horseradish peroxidase (see col. 5, line 53) conjugated anti-human IgG antibody (see col. 5, line 49).
The reference anticipates the instantly claimed invention.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 10 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pronovost et al in view3 of Wang et al (2000).

See Pronovost et al above. Pronovost et al show the utilization of a membrane solid phase (see col. 8, line 31 and col. 5, lines 25-30) for attaching at least three H.pylori proteins, as well as utilize SDS-PAGE electrophoresis for separation of the proteins into their relative molecular weights (see Pronovost et al, col. 7), but differs from the instantly claimed invention by failing to show the membrane solid phase to be PVDF and the gel separation to be carried out in a SDS-tricine gradient gel.

Wang et al shows the utilization of a PVDF membrane (see Wang et al, page 98, col. 1, paragraph 1) and an SDS-tricine gradient gel that comprises a gradient from 7.5% to 16.5% through the utilization of a 16.5% tris-tricine electrophoresis gel and a 5-20% gradient gel that would comprise the recited 7.5% gel, in an analogous art for the purpose of defining electrophoresis gel conditions for resolution of Helicobacter pylori proteins that evidence a low relative molecular weight (see Wang et al, page 97, col. 2, paragraph 3).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the composition and method of Pronovost et al with the PVDF membrane and gradient gels of Wang et al because Wang et al teaches the advantage of

obtaining greater band resolution of lower molecular weight proteins utilizing a gradient of SDS-tricine gels, and the PVDF membranes were successfully used and were readily obtainable from a commercial source (see page 96, Materials and Methods, paragraph 2.1) and were of the highest purity and quality available for the purpose of attaching H.pylori proteins to a solid phase.

In the absence of a showing of unexpected results, the person of ordinary skill in the art would have been motivated by the reasonable expectation of success of obtaining compositions that comprise at least three H.pylori proteins as taught by Pronovost et al attached to PVDF membranes as taught Wang et al , because both references produced Helicobacter pylori protein compositions attached to membranes which were readily used in subsequent methods utilizing Helicobacter pylori proteins attached to a solid phase, and Wang et al additional provides guidance and teaching for utilizing PVDF membranes as they are a ready source of solid phase, that can be sliced into individual regions if desired, and are readily available through a commercial source for blotting methods, a method taught by Pronovost et al as being useful in detecting H.pylori diagnostic antibodies.

Conclusion

23. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.
24. DeCross et al (1993) is cited (see page 386, col. 2, paragraph 4) for teaching serological testing to be the most widely available, simplest and lest expensive diagnostic test, but to have limited clinical applicability because a test can be positive and only indicate infection in the recent past, and not current infection.
25. Evans et al (1995) is cited to show a 15kd Helicobacter pylori antigen
26. Guy et al (1997) is cited to show a method of monitoring eradication therapy, that measures antibodies before (D0: time zero), during (D42) and after (D77) (see Figure 2, page 147).
27. Kumagai et al (2001) is cited to show the utilization of an 8-16% SDS-PAGE gel(see page 1284, col. 2, paragraph 1).

28. Marshall, BJ (1993, and 1995) is cited to show that antibody levels are still positive in most patients after Helicobacter infection is cured (see 1995 reference, page 796, col. 1, paragraph 1) and Figure 1 of the 1993 reference (page 184, bottom of page).
29. Laszlo et al (1992) is cited to show the determination of anti-Helicobacter pylori antibodies during eradication therapy (see English translation page 6).
30. Strauss-Ayali, D et al (May 1999) is cited to show the claimed invention but is a duplicative reference, but would be applied to the claims if necessitated by amendment.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703) 308-7543. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703)308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

Vgp
December 9, 2003

NITA MINNIFIELD
PRIMARY EXAMINER
12/15/03